Section II (Remarks)

A. Summary of Amendment to the Claims

By the present Amendment, claims 2, 3, 4, and 5 have been amended. Claims 30-39 were previously cancelled. No new matter within the meaning of 35 U.S.C. §132(a) has been introduced by the foregoing amendments.

The amendments made herein are fully consistent with and supported by the originally-filed disclosure of this application. Specifically, support for the amendment of claims 2, 3, and 4 from dependent claims to independent claims is found at page 9, ll. 10-17 of the present application.

B. Rejection Under 35 U.S.C. § 102 (a)

Claims 1-3 and 5 were rejected as purportedly being anticipated by U.S. Patent 6,319,433 to Rose et al. (hereinafter "Rose"). Specifically, the Office Action states that Rose discloses a drug unit in tablet form having 1mg of Rifalazil, which the Office contends is within the stated ranges of claims 1-3 and administered in the same form as listed in claim 5. Applicant disagrees, and traverses the rejection for the following reasons.

Claims 1-4 recite pharmaceutical compositions of rifalazil at low concentrations, with claim 1 reciting a range of from 0.1mg to 5mg, and claims 2-4 reciting ranges of 0.1-3mg, 0.1mg-1.0mg, and 0.2mg to 0.4mg, respectively. By present amendment, claims 2-4 are now independent claims.

In column 34, at line 21, claim 11 of Rose recites the administration of rifalazil once or twice a week "in dose from 1mg to about 50mg orally" (Rose, claim 11). Rose, however, does not teach administration of a 1mg dose of rifalazil in any of the clinical trials that are disclosed. ("...a single 300mg does of rifalazil..." col. 11, ll. 25-26; "...administration in dosages 0, 5, and 25 mg. a day..." col. 11, ln. 40; "weekly doses of placebo or rifalazil (25mg or 50mg)..." col. 11, ln 55; ..."receiving doses of 30mg, 100mg, and 300mg of rifalazil." col. 12, ln. 23; "administration of rifalazil as single doses (300mg, 100mg, 30mg), daily doses (25mg, 5mg) administered for 14 days, and weekly doses (50mg, 25mg) administered for 4 weeks." col. 22, ll.

55-59; "For clinical studies described above, rifalazil capsules have been prepared at several strengths; 5mg, 25mg, 50mg and 100mg." col. 32, ll. 8-11) In fact, Rose does not teach administering rifalazil at 1mg orally in tablet or capsule form anywhere in the specification.

Since Rose does not teach the oral administration in tablet or capsule form of a unit dose of rifalazil at 1mg, Rose does not anticipate the administration of rifalazil at the concentration ranges recited by claims 1-5. Accordingly, Applicants respectfully request that this rejection be withdrawn if applied to the amended claims.

C. Rejection Under 35 U.S.C. § 103

Claims 1-3, 5 and 49-51 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rose in view of Remington's Pharmaceutical Sciences (hereafter "Remington"). Specifically, the Office Action states that Rose teaches pharmaceutical compositions of rifalazil in a unit dosage amount from 1mg to 5mg for oral administration and Remington provides motivation to prepare the pharmaceutical formulation for oral administration as recited by claims 49-51. Applicants disagree and traverse the rejection for the following reasons.

As stated above, Rose does not teach administering rifalazil in a unit dosage amount of 1mg. In fact, 5 mg is the lowest concentration of rifalazil administered in the clinical trials disclosed in Rose. Additionally, the dosing regimens disclosed in Rose for treating tuberculosis involve multiple doses, at least once a week for at least 4 weeks, and potentially as long as 62 weeks (Rose, col. 31, ll. 42-44). The concentration of rifalazil disclosed for the tuberculosis treatment regimen is 10mg or 25mg, with each bi-weekly or weekly dose at the same concentration (Rose, col. 31, ll. 42-44).

In contrast, the compositions recited by claims 1-4 of the present application are from 0.1mg to 5mg, which is less than half of the concentration taught by Rose, and have significantly less side effects than the concentration amounts described in Rose (Rose, col. 15, ll. 30-34)

Further, with respect to Claim 50, the regimens taught by Rose use the same concentration for every dose, wherein the dosing regimen in claim 50, involves administering

rifalazil at a higher dose followed by a lower dose for treating the cryptic phase of a bacterial infection. (See present application, pg. 5, ll. 9-13)

The Office Action cites Remington for generically teaching therapeutic regimens wherein a higher amount of antibiotic is dispensed in a first dosage to achieve a therapeutic drug concentration quickly. Accordingly, even considering Remington for this proposition, there is no motivation to combine such a teaching with Rose, because Rose teaches that a dosing regimen with frequent doses at higher concentrations is necessary to treat the tuberculosis infection. (Rose, col. 9, ll. 25-27)

Altering the dosing regimen to *less* frequent doses in conjunction with a *lower* concentration of rifalazil for the treatment of a bacterial infection with a cryptic phase similar to tuberculosis, such as Chlamydia, is non-obvious.

Additionally, the compositions recited by claims 1-4 and the formulations recited by claims 49-51 are also non-obvious for treating a bacterial infection, where the bacteria has a cryptic phase, such as Chlamydia, in view of the currently available compositions and treatment regimens for such infections. (See present application, pg. 9, ll. 6-18) As set out in Exhibit A, the current treatments for Chlamydia are a single dose of azithromycin or a two week course of doxycycline, both treatments with significant side effects that are not found in the single dose low concentration form of rifalazil.

Azithromycin is effective against both Gram positive *and* Gram negative bacteria, which causes a greater disruption of the commensal bacterial population residing in the human digestive tract, resulting in an increased chance of developing pseudomembraneous colitis and antibiotic-resistant bacteria. Doxycycline is administered twice a day for two weeks at 100 mg, more than twenty times the amount of the single dose form of rifalazil as recited by the claims of the present application (See Exhibit A, and claims 1-5).

Accordingly, for at least the above reasons, one of skill in the art would not be motivated by the disclosure of Rose, or by the current state of the art for treating bacterial infections with persistent cryptic phases, to arrive at the compositions and the formulation recited by claims 1-5

and 49-51. As such, claims 1-5 and 49-51 are not obvious in view of Rose over Remington, and Applicants respectfully request that this rejection be withdrawn.

D. Provisional non-statutory obviousness type double patenting rejection

Claims 1-5 and 49-51 are provisionally rejected on the ground of non-statutory obviousness type double patenting over claims 43-45 of co-pending Application No. 10/948,608, over claim 4 of co-pending Application No. 11/020,870, now U.S. Patent No. 7,271,165, and over claim 4 of co-pending U.S. Application No. 11/008,597, now U.S. Patent No. 7,220,738.

Applicants respectfully request to hold these issues in abeyance until such time as patentable subject matter is achieved in the current application.

E. Fee Payable for Added Claims, Petition to Revive Fee, and RCE fee

By the present Amendment, three (3) new independent claims and one (1) multiple dependent claim have been introduced, beyond the numbers for which payment was previously made. Small entity fees payable for such added claims are calculated as follows: 3 x 110.00 = $330.00 (independent claims); and 1 x 195.00 = $195.00 (multiple dependent).

Payment of the $330.00 excess claim fee, $195.00 multiple dependent claim fee, plus the $810.00 petition fee, and the $405.00 RCE fee, results in a total fee of $1,740.00 that is authorized in the enclosed Credit Card Payment Form PTO-2038.

CONCLUSION

Based on the foregoing, all of Applicants' pending claims 1-5 and 49-51 are patentably distinguished over the art, and in form and condition for allowance. The examiner is requested to favorably consider the foregoing, and to responsively issue a Notice of Allowance. If any issues require further resolution, the examiner is requested to contact the undersigned attorney at (919) 419-9350 to discuss same.

Respectfully submitted,

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Enclosures:
Credit Card Form PTO-2038 [1 pg.]
Petition for Revival Form PTO/SB/64 [2 pg.]
RCE Transmittal Form [1 pg.]

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